REMARKS

The present application is directed to pharmaceutical compositions containing combinations of an antibody and antibody fragment, combinations of antibody fragments, and methods of treatment using the compositions for various conditions, particularly conditions caused by toxins such as botulism.

Claims 1-18 are currently pending in the application. Claims 19 and 21 were previously withdrawn, and Claims 20 and 22 were previously cancelled. Claim 1 is currently amended for clarity. No new matter has been added.

Rejection under 35 U.S.C. §102(b)

In the Office Action mailed December 15, 2008, the Examiner maintained the rejection of Claims 1-18 under 35 U.S.C. §102(b) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious over Habermann *et al.* (*Med. Microbiol. Immunol.* Vol. 161, pp. 203-210, 1975; hereinafter "Habermann"). Applicants respectfully traverse the rejections.

Habermann describes an antitoxin containing **whole** antibodies against botulinum toxins A, B, and E.

Applicants respectfully submit that Habermann fails to teach a composition containing the combination of a first binding agent, which is an antibody or a large binding fragment of an antibody, and a second binding agent, which is a small binding fragment of an antibody. In addition, Habermann fails to teach a composition having different types of binding agents that bind to the same toxin as claimed in the present application. The terms "large binding fragment" and "small binding fragment" do not mean an entire antibody as would be understood by one of skill in the art. Furthermore, the terms are also clearly defined in the specification. In paragraph [0015] of the published application, the term "large binding fragment" is defined as "an antibody fragment that comprises a significant proportion of the antibody from which it is derived....it will comprise the entire variable domain, as well as

some of a constant region (Fc). In particular, large antibody fragments include $F(ab')_2$ or $F(ab)_2$ fragments, but they may also comprise deletion mutants of an antibody sequence." In paragraph [0017] of the published application, the term "small binding fragment" is defined as "an antibody fragment which lacks a significant element of the antibody from which it is derived…In particular, small antigen binding fragments include Fab or Fab' fragments, as well as single chain (sc) antibodies, FV, VH, or VK fragments." Consequently, despite the use of the term "comprising", the claims clearly require that the composition contain a first binding agent *and* a second binding agent, wherein the second binding agent is *not* an entire antibody, though the first binding agent *may* be an entire antibody.

As noted earlier, Habermann fails to disclose a composition containing two different binding agents. Consequently, Habermann fails to disclose each and every element of, and therefore fails to anticipate, Claims 1-18. For at least the foregoing reasons, applicants respectfully assert that the rejection under 35 U.S.C. §102(b) has been overcome and request its withdrawal.

Alternative rejection under 35 U.S.C. §103(a)

With regard to the alternative rejection, under 35 U.S.C. §103(a), applicants submit that Claims 1-18 are not obvious because Habermann fails to teach, suggest or imply a composition containing fragments of an antibody. Habermann discloses a composition containing only intact antibodies as produced naturally. Furthermore there is no teaching, suggestion, or implication by Habermann to provide a composition containing two different binding agents (i.e., a whole antibody or large fragment *and* a small fragment) that bind to the *same* toxin. Nothing in Habermann indicates that using antibody fragments in a composition would produce the superior results achieved by the claimed composition.

In addition, as noted in the specification, the claimed composition has many advantages and achieves unexpectedly good benefits over the compositions described in the art, such as Habermann. First, according to paragraph [0004] of the published application, using antibody fragments instead of whole antibodies has "the advantage of producing fewer

side effects in the patients, and thus an improvement in safety." Second, paragraph [0007] of the published application states that "[c]ompositions of the invention have been found [to] provide rapid and sustained antitoxin activity" which may be due in part to the "mutually complementary properties of the first and second specific binding agents to provide sustained antitoxin capability." Habermann fails to teach this complementary combination, and specifically fails to teach the use of the second specific binding agent. The second specific binding agent, as discussed above, is a small binding fragment of an antibody, and "appears to provide an antitoxin capability that penetrates rapidly into the extravascular space to provide rapid protection" (paragraph [0008] of the specification).

For at least these reasons, applicants respectfully assert that the alternative rejection under 35 U.S.C. §103(a) has been overcome and request its withdrawal.

CONCLUSION

This response fully addresses the rejections in the Office Action mailed December 15, 2008. In light of the above remarks, applicants respectfully assert that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or if there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6591 is respectfully solicited.

No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

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